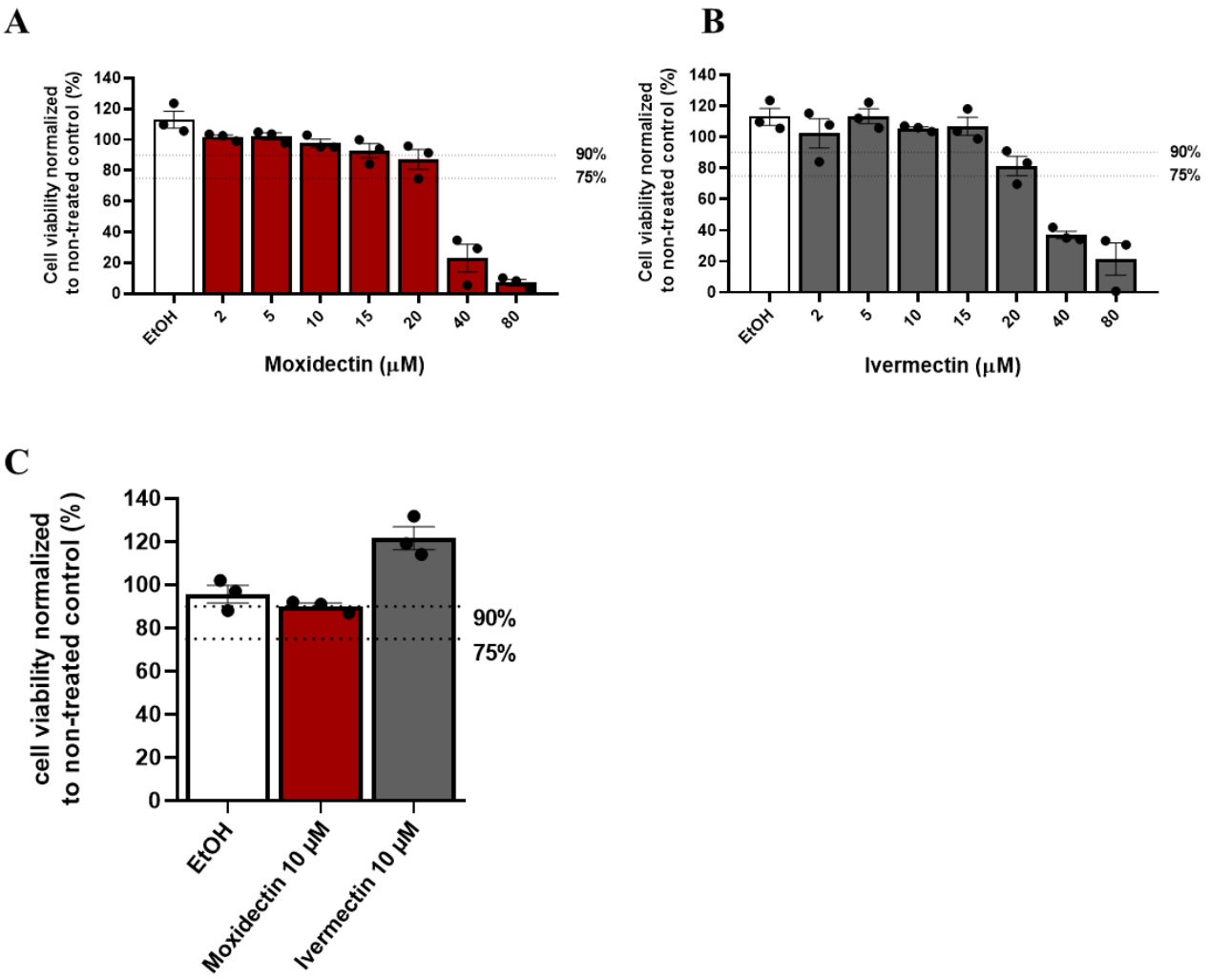
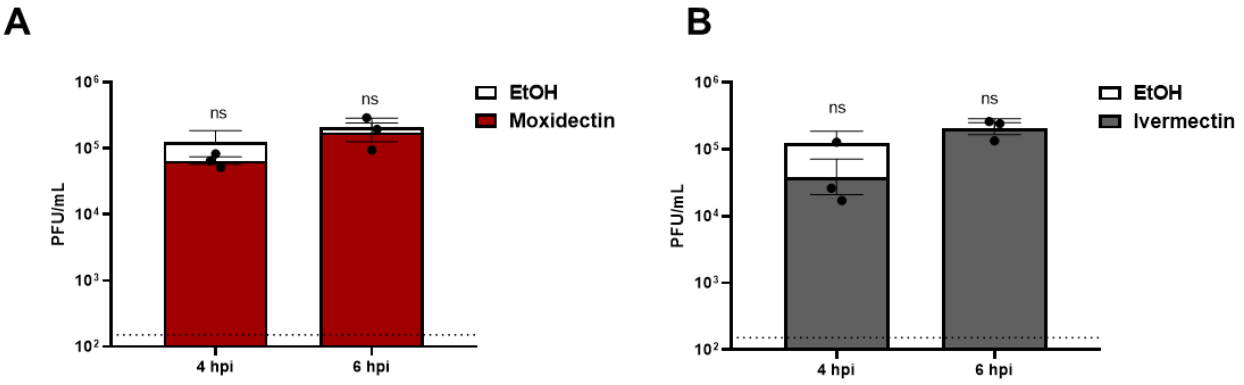
Supplementary Figures

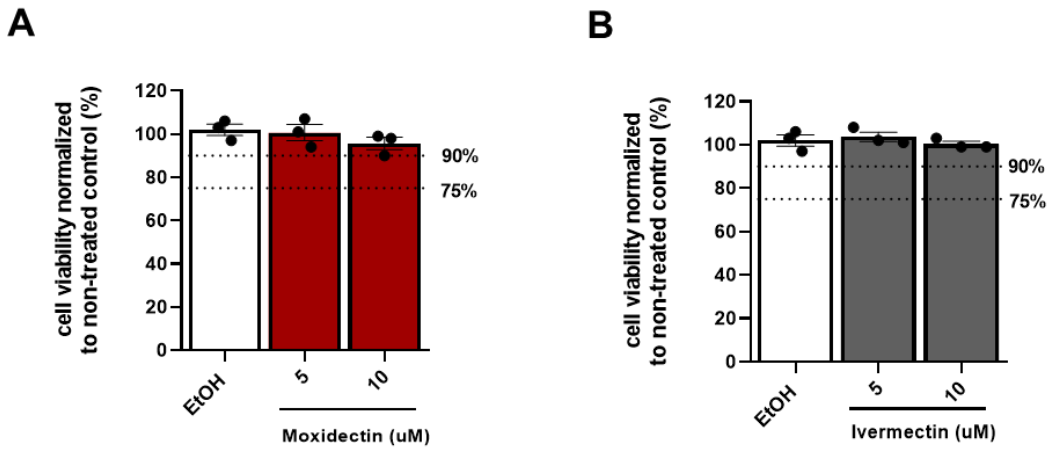


Supplemental Figure 1. Cellular cytotoxicity of moxidectin and ivermectin in Vero E6 cells. Dose-dependent cytotoxicity of (**A**) moxidectin, (**B**) ivermectin in Vero E6 cells. Cells were incubated for 8 h with increasing concentrations of the compound or equivalent volume of EtOH corresponding to the highest concentration of compound **(C)** Vero E6 cells were incubated for prolonged incubation of 60 h with moxidectin (10 µM), ivermectin (10 µM) or equivalent volumes of EtOH. Cellular cytotoxicity was determined by MTS assay. Cell survival is expressed as percentage compared to non-treated control. Each experiment was carried out

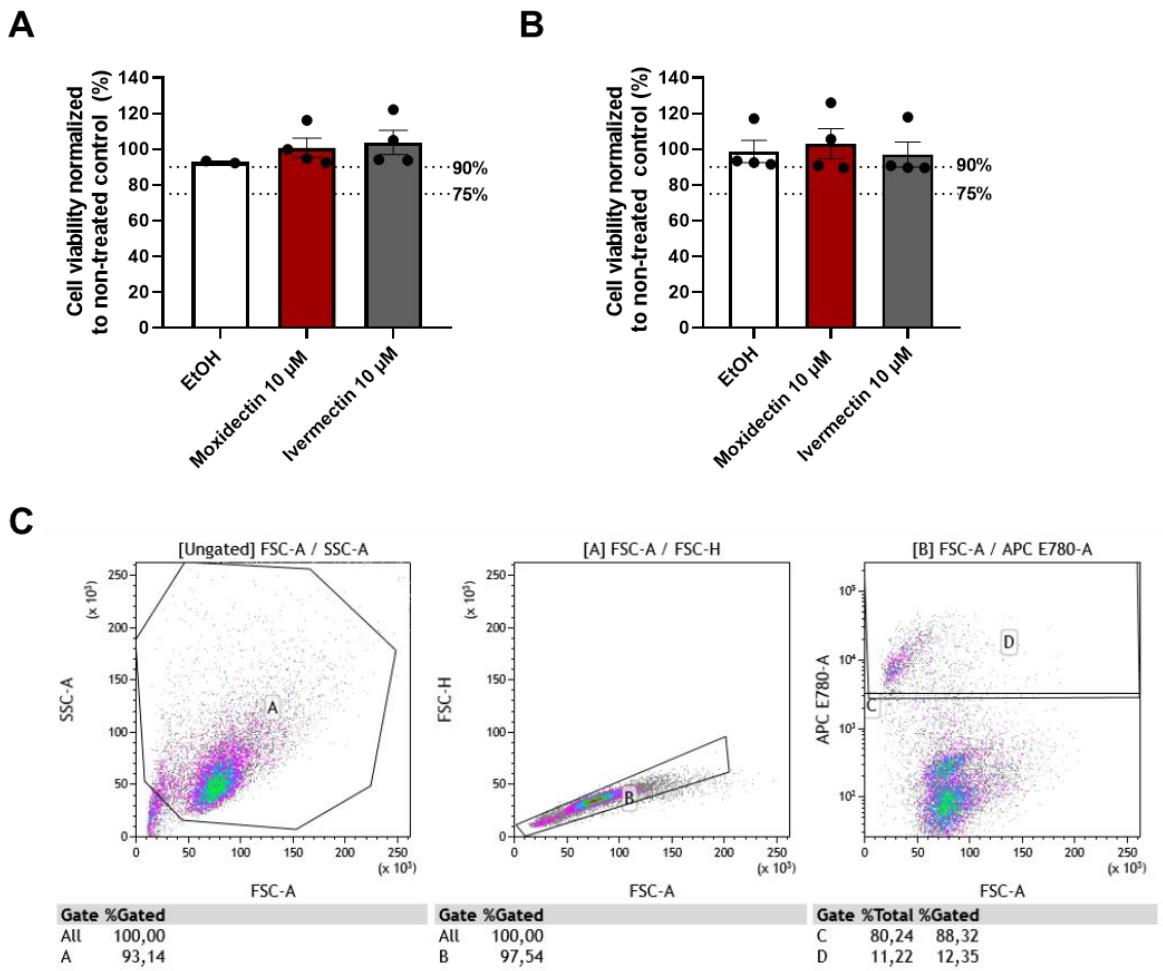
in triplicate. Each dot represents data from a single independent experiment. Data are represented as mean ± SEM of at least three independent experiments.



Supplemental Figure 2. Effect of moxidectin and ivermectin upon addition late in replication cycle of SARS-CoV-2. Vero E6 cells were infected with SARS-CoV-2 at MOI 1 for 2 h following which the inoculum was removed. Cells were treated with **(A)** moxidectin or **(B)** ivermectin at a concentration of 10 µM or the corresponding volume of EtOH at 4 or 6 hpi. At 8 hpi, cell supernatants were harvested and the virus titer was determined via plaque assay. The dotted lines indicate the detection limit of plaque assay. Each dot represents a single independent experiment from compound treated conditions. For clarity, we omitted the dots for the EtOH control samples. Data are represented as mean ± SEM of at least three independent experiments. Statistical analysis was carried out by comparing treated samples with the EtOH control using Student's t-test *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$ and ns as non-significant.



Supplemental Figure 3. Cellular cytotoxicity of moxidectin and ivermectin in Calu-3 cells. Calu-3 cells were incubated with moxidectin (5 and 10 µM), ivermectin (5 and 10 µM) or equivalent volumes of EtOH corresponding to the highest used concentration, respectively. Cellular cytotoxicity was determined by MTS assay. Cell survival is expressed as percentage compared to non-treated control. Each dot represents data from a single independent experiment. Data are represented as mean ± SEM of at least three independent experiments.



Supplemental Figure 4. Cellular cytotoxicity of moxidectin and ivermectin in PBECs. PBECs were either left untreated (NT) or incubated with 10 µM moxidectin, 10 µM ivermectin or the corresponding volume of EtOH at basolateral side for 8 hr. Cell viability was determined by flow cytometry using **(A)** viability dye and by **(B)** LDH assay. **(C)** Gating strategy used to determine live (gate C) and dead (gate D) cells in S4A. The bars in panel A show % of viable cells in EtOH and compound-treated conditions normalized to NT control. Each dot represents data from a single independent experiment. Data are represented as mean ± SEM of at least three independent experiments.